

CLAIMS

1. A method of isolating a monoclonal antibody capable of inhibiting any one of IL-3, GM-CSF and IL-5 binding to the common receptor β_c , or a receptor analogous to β_c , said method including the steps of:

immunising an animal with a cytokine receptor or portion of a cytokine containing at least the extracellular domain 4 or analogous domain in the analogous common receptor or part thereof,

isolating antibody producing cells from said animal,

fusing antibody producing cells with a myeloma cell line, and

screening for a cell line that produces the monoclonal antibody of capable of inhibiting any one of IL-3, GM-CSF and IL-5 binding to the common receptor β_c , or a receptor analogous to β_c .

2. A method as in claim 1 wherein the immunisation involves introducing a cDNA clone of a portion of or all of the common receptor including the extracellular domain 4 or analogous domain in the analogous common receptor or part thereof, into a cell and proliferating said cells to form a recombinant cell line, inoculating an animal with said recombinant cell line, isolating antibody producing cells from said animal and fusing the antibody producing cell line with a myeloma cell line to form a hybridoma cell line, screening for a hybridoma cell line that produces an antibody that binds to the recombinant cell line but not to the parent, and then testing for inhibition against all three cytokines.

3. A method as in claim 2 wherein the cell into which the cDNA clone is introduced is mammalian.

4. A method as in claim 3 wherein the mammalian cell line is a COS cell.

5. A method as in claim 2 wherein the cDNA encodes a full or partial portion of domain 4 when it is in a configuration where the F'-G' loop and/or the B'-C' loop is in its native shape.

6. A method as in claim 2 wherein the domain 4 of β_c or equivalent domain in other cytokine receptors is expressed in isolation in a microbial host and used to immunise animals for developing monoclonal antibodies.

7. A method as in claim 2 wherein the analogous receptor is any one of the cytokine superfamily receptors from the group including β_c , LIFR, gp130, IL-2R β , IL-4R/IL-13R, IL-2R γ , IL-3R α , EPOR, TPOR and OBR.
8. A method as in claim 2 wherein the method is used to isolate a monoclonal antibody that inhibits binding of all of the said receptors to a common receptor.
9. A method as in claim 7 wherein the common receptor is selected from the group of receptors acting for more than one cytokine including but not limited to gp130, LIFR, IL2R β /IL2R α , IL-4R/IL-13R and β_c .
10. A monoclonal antibody, or fragments thereof capable of inhibiting the binding of the cytokines IL-3, GM-CSF and IL-5 to the β_c receptor.
11. A monoclonal antibody as in claim 10 wherein the monoclonal antibody or fragment thereof binds to at least the F'-G' loop of domain 4 of the β_c subunit.
12. A monoclonal antibody as in claim 10 wherein the monoclonal antibody or fragment thereof binds to at least the B'-C' loop of domain 4 of the β_c subunit.
13. A monoclonal antibody as in claim 10 wherein the monoclonal antibody or fragments thereof binds to both the F'-G' as well as the B'C' loop of domain 4 of the β_c .
14. A monoclonal antibody as in claim 10 wherein the monoclonal antibody inhibits β_c receptor dimerisation.
15. A monoclonal antibody as in claim 10 wherein nucleic acid encoding the variable region of the monoclonal antibody is recombined with nucleic acid encoding non-variable regions of human origin in an expression vector.
16. A monoclonal antibody as in claim 10 wherein the inhibition leads to blocking of at least one function of all three cytokines.
17. A monoclonal antibody as in claim 10 wherein the activity leads to inhibition of stimulation of effector cell activation or survival.

18. A monoclonal antibody as in claim 17 wherein the antibody or fragment thereof is used for treatment of asthma and leads to inhibition of IL-5, IL-3 & GM-CSF mediated eosinophil activation.
19. A monoclonal antibody as in claim 17 wherein the antibody or fragment thereof is used for treatment of asthma and leads to inhibition of IL-5, IL-3 & GM-CSF mediated eosinophil survival.
20. A monoclonal antibody as in claim 17 wherein the effector cell is selected from the list including leukaemic cells, endothelial cells, breast cancer cells, prostate cancer cells, small cell lung carcinoma cells, colon cancer cells, macrophages in chronic inflammation, and dendritic cells for immunosuppression.
21. A monoclonal antibody as in claim 17 wherein the monoclonal antibody is the antibody produced by the hybridoma cell line BION-1 (ATCC HB-12525).
22. A hybridoma cell line capable of producing the monoclonal antibody of claim 10.
23. A hybridoma cell line as in claim 22 wherein the hybridoma cell line is BION-1 (ATCC HB-12525).
24. A method of isolating an inhibitor capable of competitively inhibiting the binding of BION-1 or the binding of an agent capable of inhibiting BION-1 binding, to the β_c subunit, the method including the steps of contacting BION-1 or fragment thereof with the β_c subunit or fragment thereof as well as a candidate inhibitory compound,
and measuring the degree of binding.
25. A method as in claim 24 wherein a reporting means is provided to facilitate the detection of binding of BION1 or fragment thereof with β_c subunit or fragment thereof.
26. A method as in claim 24 wherein the inhibitor is a peptide or a nucleotide molecule.
27. An inhibitor isolated by the method of claim 24.

28. A cytokine inhibitor that simultaneously blocks the binding of β_c by IL-3, GM-CSF, and IL-5.
29. An inhibitor of leukaemic cell proliferation wherein the inhibitor inhibits binding of IL-3, GM-CSF and IL-5 with β_c subunit or fragment thereof.
30. An inhibitor as in claim 29 wherein the proliferation of the cell is cytokine dependent.
31. An inhibitor as in claim 29 wherein the inhibitor is BION-1 or an agent capable of inhibiting BION-1 binding with β_c subunit or fragment thereof.